

REC'D PCT/AUTO 26 SEP 2005
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105-0032

**DECLARATION AND
POWER OF ATTORNEY
FOR UTILITY OR DESIGN
PATENT APPLICATION
(37 CFR 1.63)**

Declaration Submitted with Initial Filing

OR

Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required)

| | |
|--------------------------|--------------------------|
| Attorney Docket Number | 21135PV 10/521006 |
| First Named Inventor | Steven S. Carroll et al. |
| COMPLETE IF KNOWN | |
| Application Number | |
| Filing Date | |
| Group Art Unit | |
| Examiner Name | |

As a below named inventor, I hereby declare that:

My residence, mailing address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

NUCLEOSIDE DERIVATIVES AS INHIBITORS OF RNA-DEPENDENT RNA VIRAL POLYMERASE

(Title of the Invention)

the specification of which

bears the Attorney Docket Number and Title of the Invention noted above

OR

is attached hereto

OR

was filed on (MM/DD/YYYY) [REDACTED] as United States Application Number or PCT International

Application Number [REDACTED] and was amended on (MM/DD/YYYY) [REDACTED] (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

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I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) of any foreign application(s) for patent or inventor's certificate(s), or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate(s), or of any PCT international application having a filing date before that of the application on which priority is claimed.

| Prior Foreign Application Number(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Attorney Docket Number | Priority Claimed? YES <input type="checkbox"/> NO <input type="checkbox"/> |
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Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

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| 60/396,252 | 07/16/2002 | 21135PV |
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| U.S. Parent Application or PCT Parent Application Number | Parent Filing Date (MM/DD/YYYY) | Parent Patent Number (if applicable) |
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| PCT/US03/21589 | 07/11/2003 | |
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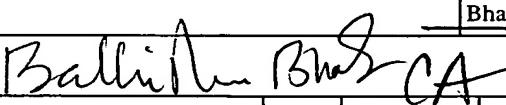
Practitioners Associated with the Customer Number **000210**
 OR
 Registered practitioner(s) named below

| Name | Registration Number | Name | Registration Number |
|---------------------|---------------------|----------------|---------------------|
| Philippe L. Durette | 35,125 | Melvin Winokur | 32,763 |
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| Address | Merck & Co., Inc. - Patent Department | | | | |
| Address | P.O. Box 2000, RY60-30 | | | | |
| City | Rahway | | State | NJ | ZIP |
| Country | USA | Telephone | (732)594-4568 | Fax | (732)594-4720 |

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| Given Name (first and middle [if any]) | Family Name or Surname | | | | |
| Balkrishen | Bhat | | | | |
| Inventor's Signature |  | | Date | March 7, 2005 | |
| Residence: City | Carlsbad | State | CA | Country | USA |
| Mailing Address | ISIS Pharmaceuticals, 2292 Faraday Avenue | | | | |
| City | Carlsbad | State | CA | ZIP | 92008 |
| | | | | Country | USA |

Additional inventors are being named on the 2 supplemental Additional Inventors(s) sheet(s) PTO/SB/02A attached hereto.

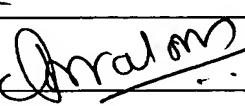
DECLARATION AND POWER OF ATTORNEY

ADDITIONAL INVENTOR(S)
Supplemental Sheet

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| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Steven S. | | Carroll | | | | | |
| Inventor's Signature | <i>PA</i> | | | | Date | | |
| Residence: City | Yardley | State | PA | Country | USA | Citizenship | US |
| Mailing Address | Merck Research Laboratories, Sumneytown Pike, P.O. Box 4 | | | | | | |
| City | West Point | State | PA | ZIP | 19486 | Country | U.S.A. |
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| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Anne B. | | Eldrup | | | | | |
| Inventor's Signature | <i>CT</i> | | | | Date | | |
| Residence: City | Danbury | State | CT | Country | USA | Citizenship | DK |
| Mailing Address | ISIS Pharmaceuticals, 2292 Faraday Avenue | | | | | | |
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| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Malcolm | | MacCoss | | | | | |
| Inventor's Signature | <i>NJ</i> | | | | Date | | |
| Residence: City | Freehold | State | NJ | Country | USA | Citizenship | GB |
| Mailing Address | Merck & Co., Inc. P.O. Box 2000 | | | | | | |
| City | Rahway | State | NJ | ZIP | 07065-0907 | Country | U.S.A. |
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| Thazha P. | | Prakash | | | | | | |
| Inventor's Signature |  | | | CA | Date | 3 - 4 - 05 | | |
| Residence: City | Carlsbad | State | CA | Country | USA | Citizenship | IN | |
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Practitioners Associated with the Customer Number **000210**
 OR
 Registered practitioner(s) named below

| Name | Registration Number | Name | Registration Number |
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| | | | | Country | USA |

Additional inventors are being named on the 2 supplemental Additional Inventors(s) sheet(s) PTO/SB/02A attached hereto.

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**ADDITIONAL INVENTOR(S)
Supplemental Sheet**

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| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
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| Inventor's Signature | | | | | Date | | | |
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| Mailing Address | Merck Research Laboratories, Sumneytown Pike, P.O. Box 4 | | | | | | | |
| City | West Point | State | PA | ZIP | 19486 | Country | U.S.A. | |
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| Malcolm | | MacCoss | | | | | | |
| Inventor's Signature | <i>Malcolm MacCoss</i> | | | | Date | <i>Jan 26, 2005</i> | | |
| Residence: City | Freehold | State | NJ | Country | USA | Citizenship | GB | |
| Mailing Address | Merck & Co., Inc. P.O. Box 2000 | | | | | | | |
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| | | | | | | | |
|--|---|---|----|---------|------------|-------------|--------|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Steven S. | | Carroll | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | Yardley | State | PA | Country | USA | Citizenship | US |
| Mailing Address | Merck Research Laboratories, Sumneytown Pike, P.O. Box 4 | | | | | | |
| City | West Point | State | PA | ZIP | 19486 | Country | U.S.A. |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Anne B. | | Eldrup | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | Danbury | State | CT | Country | USA | Citizenship | DK |
| Mailing Address | ISIS Pharmaceuticals, 2292 Faraday Avenue | | | | | | |
| City | Carlsbad | State | CA | ZIP | 92008 | Country | USA |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Malcolm | | MacCoss | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | Freehold | State | NJ | Country | USA | Citizenship | GB |
| Mailing Address | Merck & Co., Inc. P.O. Box 2000 | | | | | | |
| City | Rahway | State | NJ | ZIP | 07065-0907 | Country | U.S.A. |
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| David B. | | Olsen | | | | | |
| Inventor's Signature |  | | | | Date | 21 Jan 05 | |
| Residence: City | Lansdale | State | PA | Country | USA | Citizenship | US |
| Mailing Address | Merck Research Laboratories, Sumneytown Pike, P.O. Box 4 | | | | | | |
| City | West Point | State | PA | ZIP | 19486 | Country | U.S.A. |

DECLARATION AND POWER OF ATTORNEY**ADDITIONAL INVENTOR(S)
Supplemental Sheet**

| | | | | | | | | |
|--|--|---|----|------------------------|-------|-------------|-----|--|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | | | Family Name or Surname | | | | |
| Thazha P. | | Prakash | | | | | | |
| Inventor's Signature | | | | | Date | | | |
| Residence: City | Carlsbad | State | CA | Country | USA | Citizenship | IN | |
| Mailing Address | ISIS Pharmaceuticas, 2292 Faraday Avenue | | | | | | | |
| City | Carlsbad | State | CA | ZIP | 92008 | Country | USA | |
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| Inventor's Signature | | | | | Date | | | |
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| Given Name (first and middle [if any]) | | | | Family Name or Surname | | | | |
| Inventor's Signature | | | | | Date | | | |
| Residence: City | | State | | Country | | Citizenship | | |
| Mailing Address | | | | | | | | |
| City | | State | | ZIP | | Country | | |

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[Page 4 of 4]

| | | | |
|---|--|------------------------|--------------------------|
| DECLARATION AND POWER OF ATTORNEY FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63) | | Attorney Docket Number | 21135P |
| | | First Named Inventor | Steven S. Carroll et al. |
| COMPLETE IF KNOWN | | | |
| | | Application Number | |
| | | Filing Date | |
| | | Group Art Unit | |
| | | Examiner Name | |

As a below named inventor, I hereby declare that:

My residence, mailing address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

NUCLEOSIDE DERIVATIVES AS INHIBITORS OF RNA-DEPENDENT RNA VIRAL POLYMERASE

(Title of the Invention)

the specification of which

bears the Attorney Docket Number and Title of the Invention noted above

OR

is attached hereto

OR

was filed on (MM/DD/YYYY) as United States Application Number or PCT International

Application Number and was amended on (MM/DD/YYYY) (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) of any foreign application(s) for patent or inventor's certificate(s), or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate(s), or of any PCT international application having a filing date before that of the application on which priority is claimed.

| Prior Foreign Application Number(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Attorney Docket Number | Priority Claimed? YES <input type="checkbox"/> NO <input type="checkbox"/> |
|-------------------------------------|---------|----------------------------------|------------------------|---|
| | | | | |
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| | | | | |
| | | | | |

Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

| Application Number(s) | Filing Date (MM/DD/YYYY) | Attorney Docket Number |
|-----------------------|--------------------------|------------------------|
| 60/396,252 | 07/16/2002 | 21135PV |
| | | |
| | | |
| | | |

'DECLARATION AND POWER OF ATTORNEY for Utility or Design Patent Application

I hereby claim the benefit under 35 U.S.C 120 of any United States application(s), or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information known to me to be material to patentability as defined in 37 CFR 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

| U.S. Parent Application or PCT Parent Application Number | Parent Filing Date (MM/DD/YYYY) | Parent Patent Number (if applicable) |
|--|---------------------------------|--------------------------------------|
| PCT/US03/21589 | 07/11/2003 | |
| | | |
| | | |
| | | |
| | | |

Additional U.S. or PCT international application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

As a named inventor, I hereby appoint, respectively and individually, as my attorney(s) or agent(s) with full power of substitution and revocation, the following registered practitioner(s) to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith:

Practitioners Associated with the Customer Number 000210
 OR
 Registered practitioner(s) named below

| Name | Registration Number | Name | Registration Number |
|---------------------|---------------------|----------------|---------------------|
| Philippe L. Durette | 35,125 | Melvin Winokur | 32,763 |
| | | | |
| | | | |
| | | | |
| | | | |

Direct all correspondence to: Customer Number 000210

| | | | | | |
|---------|---------------------------------------|-----------|---------------|-----|-------------------|
| Name | Philippe L. Durette | | | | |
| Address | Merck & Co., Inc. - Patent Department | | | | |
| Address | P.O. Box 2000, RY60-30 | | | | |
| City | Rahway | State | NJ | ZIP | 07065-0907 |
| Country | USA | Telephone | (732)594-4568 | | Fax (732)594-4720 |

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

| | | | | | | | |
|--|---|-------|------------------------|---------|-------|-------------|-----|
| Name of Sole or First Inventor: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | | Family Name or Surname | | | | |
| Balkrishen | | | Bhat | | | | |
| Inventor's Signature | | | | Date | | | |
| Residence: City | Carlsbad | State | CA | Country | USA | Citizenship | IN |
| Mailing Address | ISIS Pharmaceuticals, 2292 Faraday Avenue | | | | | | |
| City | Carlsbad | State | CA | ZIP | 92008 | Country | USA |
| <input checked="" type="checkbox"/> Additional inventors are being named on the <u>2</u> supplemental Additional Inventors(s) sheet(s) PTO/SB/02A attached hereto. | | | | | | | |

DECLARATION AND POWER OF ATTORNEY**ADDITIONAL INVENTOR(S)
Supplemental Sheet**

| | | | | | | | | |
|--|--|---|----|------------------------|------------|-------------|--------------|--|
| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | | |
| Given Name (first and middle [if any]) | | | | Family Name or Surname | | | | |
| Steven S. | | Carroll | | | | | | |
| Inventor's Signature | | | | | | Date | | |
| Residence: City | Yardley | State | PA | Country | USA | Citizenship | US | |
| Mailing Address | Merck Research Laboratories, Sumneytown Pike, P.O. Box 4 | | | | | | | |
| City | West Point | State | PA | ZIP | 19486 | Country | U.S.A. | |
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| Given Name (first and middle [if any]) | | | | Family Name or Surname | | | | |
| Anne B. | | Eldrup | | | | | | |
| Inventor's Signature | | | | | | Date | March 3/2005 | |
| Residence: City | Danbury | State | CT | Country | USA | Citizenship | DK | |
| Mailing Address | ISIS Pharmaceuticals, 2292 Faraday Avenue | | | | | | | |
| City | Carlsbad | State | CA | ZIP | 92008 | Country | USA | |
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| Malcolm | | MacCoss | | | | | | |
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| City | Rahway | State | NJ | ZIP | 07065-0907 | Country | U.S.A. | |
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| City | West Point | State | PA | ZIP | 19486 | Country | U.S.A. | |

DECLARATION AND POWER OF ATTORNEY

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| Name of Additional Joint Inventor, if any: | | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | | |
| Given Name (first and middle [if any]) | | Family Name or Surname | | | | | |
| Thazha P. | | Prakash | | | | | |
| Inventor's Signature | | | | | Date | | |
| Residence: City | Carlsbad | State | CA | Country | USA | Citizenship | IN |
| Mailing Address | ISIS Pharmaceuticals, 2292 Faraday Avenue | | | | | | |
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| Inventor's Signature | | | | | Date | | |
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| Mailing Address | | | | | | | |
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| DECLARATION AND POWER OF ATTORNEY FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63) | | Attorney Docket Number | 21135P |
| | | First Named Inventor | Steven S. Carroll et al. |
| COMPLETE IF KNOWN | | | |
| | | Application Number | |
| | | Filing Date | |
| | | Group Art Unit | |
| | | Examiner Name | |

Declaration Submitted with Initial Filing Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required) OR

As a below named inventor, I hereby declare that:

My residence, mailing address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

NUCLEOSIDE DERIVATIVES AS INHIBITORS OF RNA-DEPENDENT RNA VIRAL POLYMERASE

(Title of the Invention)

the specification of which
 bears the Attorney Docket Number and Title of the Invention noted above

OR
 is attached hereto
 OR
 was filed on (MM/DD/YYYY) [] as United States Application Number or PCT International

Application Number [] and was amended on (MM/DD/YYYY) [] (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) of any foreign application(s) for patent or inventor's certificate(s), or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate(s), or of any PCT international application having a filing date before that of the application on which priority is claimed.

| Prior Foreign Application Number(s) | Country | Foreign Filing Date (MM/DD/YYYY) | Attorney Docket Number | Priority Claimed? YES NO |
|-------------------------------------|---------|----------------------------------|------------------------|---|
| | | | | <input type="checkbox"/> <input type="checkbox"/> |
| | | | | <input type="checkbox"/> <input type="checkbox"/> |
| | | | | <input type="checkbox"/> <input type="checkbox"/> |
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| 60/396,252 | 07/16/2002 | 21135PV |
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| U.S. Parent Application or PCT Parent Application Number | Parent Filing Date (MM/DD/YYYY) | Parent Patent Number (if applicable) |
|--|---------------------------------|--------------------------------------|
| PCT/US03/21589 | 07/11/2003 | |
| | | |
| | | |
| | | |
| | | |

Additional U.S. or PCT international application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

As a named inventor, I hereby appoint, respectively and individually, as my attorney(s) or agent(s) with full power of substitution and revocation, the following registered practitioner(s) to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith:

Practitioners Associated with the Customer Number **000210**
 OR
 Registered practitioner(s) named below

| Name | Registration Number | Name | Registration Number |
|---------------------|---------------------|----------------|---------------------|
| Philippe L. Durette | 35,125 | Melvin Winokur | 32,763 |
| | | | |
| | | | |
| | | | |

Direct all correspondence to: Customer Number **000210**

| | | | | | |
|---------|---------------------------------------|-----------|---------------|-----|---------------|
| Name | Philippe L. Durette | | | | |
| Address | Merck & Co., Inc. - Patent Department | | | | |
| Address | P.O. Box 2000, RY60-30 | | | | |
| City | Rahway | State | NJ | ZIP | 07065-0907 |
| Country | USA | Telephone | (732)594-4568 | Fax | (732)594-4720 |

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

| | | | | | |
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| Name of Sole or First Inventor: | <input type="checkbox"/> A petition has been filed for this unsigned inventor | | | | |
| Given Name (first and middle [if any]) | Family Name or Surname | | | | |
| Balkrishen | Bhat | | | | |
| Inventor's Signature | | | | Date | |
| Residence: City | Carlsbad | State | CA | Country | USA |
| Mailing Address | Citizenship | | | | |
| City | Carlsbad | State | CA | ZIP | 92008 |
| | | | | Country | USA |
| <input checked="" type="checkbox"/> Additional inventors are being named on the <u>2</u> supplemental Additional Inventors(s) sheet(s) PTO/SB/02A attached hereto. | | | | | |

DECLARATION AND POWER OF ATTORNEY

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| Steven S. | | Carroll | | | | | | |
| Inventor's Signature | <i>Steve S. Carroll</i> | | | | | Date | 21 January 2005 | |
| Residence: City | Yardley | State | PA | Country | USA | Citizenship | US | |
| Mailing Address | Merck Research Laboratories, Sumneytown Pike, P.O. Box 4 | | | | | | | |
| City | West Point | State | PA | ZIP | 19486 | Country | U.S.A. | |
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| Mailing Address | ISIS Pharmaceuticals, 2292 Faraday Avenue | | | | | | | |
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| Malcolm | | MacCoss | | | | | | |
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DECLARATION AND POWER OF ATTORNEY

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| Thazha P. | | Prakash | | | | | |
| Inventor's Signature | | | | | Date | | |
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| Residence: City | | State | | Country | | Citizenship | |
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